
Pluripotent stem cell energy metabolism: an update.

Journal: EMBO J

Publication Year: 2015

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PubMed link: 25476451

Funding Grants: Mitochondrial Metabolism in hESC and hiPSC Differentiation, Reprogramming, and Cancer

Public Summary:

Recent studies link changes in energy metabolism with the fate of pluripotent stem cells (PSCs). Safe use of PSC derivatives in regenerative medicine requires an enhanced understanding and control of factors that optimize in vitro reprogramming and differentiation protocols. Relative shifts in metabolism from naive through "primed" pluripotent states to lineage-directed differentiation place variable demands on mitochondrial biogenesis and function for cell types with distinct energetic and biosynthetic requirements. In this context, mitochondrial respiration, network dynamics, TCA cycle function, and turnover all have the potential to influence reprogramming and differentiation outcomes. Shifts in cellular metabolism affect enzymes that control epigenetic configuration, which impacts chromatin reorganization and gene expression changes during reprogramming and differentiation. Induced PSCs (iPSCs) may have utility for modeling metabolic diseases caused by mutations in mitochondrial DNA, for which few disease models exist. Here, we explore key features of PSC energy metabolism research in mice and man and the impact this work is starting to have on our understanding of early development, disease modeling, and potential therapeutic applications.

Scientific Abstract:

Recent studies link changes in energy metabolism with the fate of pluripotent stem cells (PSCs). Safe use of PSC derivatives in regenerative medicine requires an enhanced understanding and control of factors that optimize in vitro reprogramming and differentiation protocols. Relative shifts in metabolism from naive through "primed" pluripotent states to lineage-directed differentiation place variable demands on mitochondrial biogenesis and function for cell types with distinct energetic and biosynthetic requirements. In this context, mitochondrial respiration, network dynamics, TCA cycle function, and turnover all have the potential to influence reprogramming and differentiation outcomes. Shifts in cellular metabolism affect enzymes that control epigenetic configuration, which impacts chromatin reorganization and gene expression changes during reprogramming and differentiation. Induced PSCs (iPSCs) may have utility for modeling metabolic diseases caused by mutations in mitochondrial DNA, for which few disease models exist. Here, we explore key features of PSC energy metabolism research in mice and man and the impact this work is starting to have on our understanding of early development, disease modeling, and potential therapeutic applications.

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